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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,022	11/24/1998	SILVIO DE FLORA	P8903-8035	7341

7590 12/31/2002  
OBLON, SPIVACK, McCLELLAND, MAIER & NEUSTADT, P.C.  
1755 Jefferson Davis Highway  
Fourth Floor  
Arlington, VA 22202

EXAMINER

OWENS JR, HOWARD V

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 12/31/2002

38

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

09/125,022

Applicant(s)

DE FLORA ET AL.

Examiner

Howard V Owens

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 July 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

### Detailed Action

The following is in response to the appeal brief filed 7/19/02:

An action on the merits of claims 13-15 is contained herein below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### Withdrawal of Finality

Pursuant to an appeals conference, the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

The finality of the last action is withdrawn.

### 35 U.S.C. 102(b)

Claims 13 - 15 are rejected under 35 U.S.C. 102(b) as being anticipated by either Freeman et al. (Freeman), *Toxicology and Applied Pharmacology*, vol. 54, pp. 168-175 or Doroshov et al. (Doroshov), *J. Clinical Investigation*, vol. 68, pp. 1053 - 64.

The claims are directed to a method for inhibiting formation of a metastasis in a patient having a primary cancerous tumor, which has not yet metastasized but is capable of metastasizing, comprising the administration of a synergistically effective amount of N-acetyl-cysteine and doxorubicin. Claim 14 specifies that the dosage of N-acetylcysteine be between 100 mg and 6g/day. Claim 15 requires that the doxorubicin be administered in an amount of between 1 and 50 mg per dose.

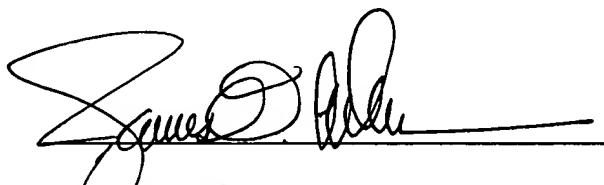
Freeman teaches that doxorubicin (adriamycin) is a potent anticancer agent which is useful in treatment of malignant lymphomas. Malignant is defined as "tending to produce death or deterioration; tending to infiltrate, metastasize, and terminate fatally"; therefore the use of doxorubicin to treat tumors which have not yet metastasized had been clearly set forth in the prior art (p.168). Freeman anticipates the combination of

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doxorubicin and N-acetylcysteine in the treatment of cancer in the dosage ranges that overlap with applicant's ranges (see table 1). Moreover, the improved chemotherapeutic efficacy or synergism of doxorubicin when combined with N-acetylcysteine is taught by Freeman as it teaches (p.174, col.1-2), *"In fact, at the lower dose of adriamycin, the increase in life span was even greater with concurrent administration of the sulfhydryl compounds, which suggests that the adriamycin-sulfhydryl compound combination potentiates the antineoplastic effect of adriamycin"*. The instant claim language is drawn to a tumor that "has not yet metastasized, but is capable of metastasizing.."; therefore, any teachings by Freeman that are drawn to the combination of doxorubicin and N-acetylcysteine to inhibit cancer growth are anticipatory; moreover, it is inherent to administer an anticancer compound to a tumor to inhibit the growth of the tumor or eradicate the tumor so that metastasis does not occur.

Doroshow anticipates the claims cited supra as it teaches the combination of n-acetylcysteine and doxorubicin in the treatment of tumors (pp. 1053-1054) within the claimed dosage range. Doroshow teaches the synergistic effect as it teaches that pretreatment with n-acetylcysteine significantly reduced long term mortality in animals receiving doses of doxorubicin and that n-acetylcysteine may provide a means to enhance the chemotherapeutic index of doxorubicin.

Howard V. Owens  
Patent Examiner  
Art Unit 1623



James O. Wilson  
Supervisory Patent Examiner  
Technology Center 1600

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.